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Original Research Article

A prospective study to assess glycemic status as a possible prognostic marker in non diabetic acute organophosphate poisoning patients

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ABSTRACT

Background: Organophosphates (OP) are a diverse group of insecticides used for pest control. Due to easy availability of these compounds over the counter, organophosphate poisoning continues to be a major cause of deliberate self-harm. Although choline esterase inhibition plays a key role in OP poisoning, other metabolic factors like dysglycemia contribute to the severity of poisoning. The present study attempts to assess glycaemic variability as a probable prognostic factor in acute OP poisoning. Aim of the study was to correlate the blood glucose levels with the severity and treatment outcome of acute organophosphate poisoning.
Methods: 100 patients of acute organophosphate poisoning admitted in the hospitals affiliated to Bangalore Medical College and Research Institute during the study period from August 2018 to July 2019, were enrolled into the study as per the inclusion criteria and graded into mild, moderate & severe, based on Peradeniya organophosphorus poisoning (POP) scale. Random blood sugar (RBS) was estimated at the time of admission and patients were followed up till recovery/death.
Results: The patients in this study were categorized into hypoglycemics (10%), euglycemics (75%) and hyperglycemic (15%). 16% of euglycemics, 30% of hypoglycemics and 60% of hyperglycemics had severe grade of poisoning. The ventilator requirements in hypoglycaemics, euglycemics and hyperglycemics were 40%,48% and 80% respectively. The outcome in terms of mortality was 8% in euglycemics group and 20% in hyperglycemics group. Hence hyperglycemia was found to be a poor prognostic marker in acute organophosphate poisoning.
Conclusions: RBS at admission in acute organophosphate poisoning patients is a simple, inexpensive tool that may help to predict the clinical outcome. Early identification of the poor prognostic indicators may help in timely intervention, to reduce morbidity and mortality, especially in a resource limited country like India.

Keywords: Hyperglycaemia, Organophosphate compound poisoning, Peradeniya organophosphorus poisoning score, Random blood glucose

INTRODUCTION

Organophosphates are a diverse group of insecticides used for pest control both in agriculture as well as in household gardens.[1] Ingestion of organophosphates in an attempt to commit suicide is a major problem, especially in a developing country like India, as these items are easily available over the counter.[2] This ease of availability of the compounds has resulted in a gradual increase in accidental and suicidal poisoning with the compound. It accounts for 80% of pesticide related hospital admissions and nearly two third of self-harm deaths.[2] Insecticide consumption is one of the most

common mode of committing suicide followed by hanging in India and they are more common among males (70.54%) followed by females (29.47%).[3] The mortality rate of acute organophosphate poisoning is 10-20% and the World Health Organization (WHO) has estimated that 200,000 people die each year from pesticide poisoning. Death is usually a result of respiratory paralysis or due to asphyxia secondary to aspiration of bronchial secretions, bronchoconstriction, cardiac arrhythmias or rarely pulmonary oedema.

Organophosphate compounds act by inhibiting acetyl cholinesterase enzyme causing increased concentration of acetylcholine leading to muscarinic and nicotinic receptor overactivity.[4] Although choline esterase inhibition plays a key role in organophosphate poisoning, other metabolic factors are also important, one such contributing factor for the severity of organophosphate compound poisoning is dysglycemia. A variety of glycemic changes ranging from hypoglycemia to hyperglycemia and rarely ketoacidosis in Organophosphate poisoning are reported.[5] Besides neurotoxicity, organophosphate induced endocrine toxicity, immunotoxicity, reproductive toxicity, genotoxicity, disruption of cellular oxidative balance and glucose homeostasis are being studied.[5]

In the background of a high burden of acute organophosphate poisoning in a developing country like India, with limited facilities for its diagnosis and treatment, it continues to be a major public health problem. Despite advancements in its management, mortality among organophosphate poisoning patients is on the rise. A growing body of evidence suggests that, variations in the glycemic status is associated with increased morbidity and mortality, with greater ventilator requirement.[5] Early identification of the poor prognostic indicators may help in timely intervention so as to bring down the complications and mortality. Further research in this regard may provide a more comprehensive view of illness severity and an insight into potential etiology. Moreover, random blood glucose is a simple, inexpensive tool that may help to predict the treatment outcome of acute organophosphate poisonings.

Objectives of the study was to estimate random blood sugar levels in cases of acute organophosphate compound poisoning at the time of admission and to correlate the blood sugar levels with the severity to organophosphate poisoning and clinical outcome.

METHODS

This prospective analytical study was conducted in the Department of Internal Medicine, of Victoria and Bowring and Lady Curzon hospitals attached to BMC and RI over a period of one year from August 2018 to July 2019. A total of 100 patients with definite history of ingestion of organophosphate compound with no known comorbidities, admitted to the hospital directly within 12 hours of ingestion were enrolled.

After obtaining institutional ethics committee clearance and written informed consent, the patients were subjected to inclusion and exclusion criteria. A detailed history and clinical evaluation was done for all the enrolled patients. All patients were investigated with routine and specific lab tests, including baseline RBS, HbA1c, pseudocholinesterase levels and other relevant tests at admission. Patients with HbA1c >6.4% at admission were excluded from the study. All patients were treated as per standard protocol, initially in the emergency room and later patients requiring ICU care, were shifted to the medical ICU. Early stomach wash was administered to all patients. Stomach and other body fluid samples were preserved and sent to forensic lab for analysis, for medicolegal purposes. Based on RBS levels at admission, patients were grouped into three categories-hypoglycemics (RBS<70mg/dL), euglycemics and hyperglycemics (>140 mg/dL) and the severity and outcome were compared among the 3 groups. Patients were graded clinically into mild, moderate and severe based on Peradeniya Organophosphorus Poisoning Scale scoring (Table 1) and were followed up until the outcome (recovery or death).[5] The discharged patients were followed up with regular medical check-ups and psychiatric counselling upto 1 month.

Table 1: Peradeniya organophosphorus poisoning scale (POP scale).[5]

Parameter	Criteria	Score
Pupil size	≥2mm	0
	<2mm	1
	Pinpoint	2
Respiratory rate	<20 cpm	0
	≥20 cpm	1
	≥20 cpm with central cyanosis	2
Heart rate	>60 bpm	0
	41-60 bpm	1
	<40 bpm	2
Fasciculations	None	0
	Present, generalised/continuous	1
	Both generalised and continuous	2
Level of consciousness	Conscious and rational	0
	Impaired response to verbal command	1
	No response to verbal command	2
Seizures	Absent	0
	Present	1

Mild grade:0-3 score; Moderate grade:4-7 score; Severe grade: 8-11 score.

Statistical analysis

Data was analysed by descriptive statistics, Student's T test being used to see significant difference between 2 groups. ANOVA test was used to compare ≥3 groups.

Chi square test was used to analyse association between the quantitative variables

RESULTS

A total of 100 patients were enrolled into the study, and 70% of them were males. Maximum number of patients (54 patients) were aged between 18 to 30 years. The youngest patient of our study was aged 18 years and the oldest patient aged 82 years. The mean age group of our patients was 41.4 years. Mean duration of the distance travelled by the patient to this tertiary health care centre was 3 hours. In all patients the mode of OP poisoning was by ingestion with suicidal intent. Out of the 100 patients enrolled, 44 patients presented to the emergency room within 6 hours of ingestion and the rest 66 patients presented between 6 to 12 hours. 66 out of the 100 were from a rural background, with 58 using OPs for agricultural purposes. Majority of the patients (88 patients) had committed suicide for the first time as an impulsive act, whereas 7 patients had attempted suicide for the 2nd time and the rest 5 patients had attempted for the 3rd time. In our study most commonly used organophosphate compound was Triazophos followed by Dimethoate and Monocrotophos, 52 out of the 100 patients were intubated while the rest 48 patients did not require intubation. Among those intubated, 36 patients were intubated on the day of admission,10 patients were intubated on the 2nd day, 3 patients were intubated on the 3rd day of admission and 3 more intubated on 4th day and beyond. The mean duration of hospital stay was 4.32 days among those not intubated and 12.4 days among those intubated.

Based on the clinical severity assessed by POP scoring, 49 patients had mild grade, 27 patients had moderate grade and the rest 24 patients had severe grade of poisoning.

Table 2: Cross-tabulation of pop score and intubation.

	POP score				p value
	Intubation	**Mild**	**Moderate**	**Severe**	**Total**	
Females	Not intubated	14	2	0	16	0.00*
	Intubated	1	8	5	14	
	Total	15	10	5	30	
Males	Not intubated	29	3	0	32	0.00*
	Intubated	5	14	19	38	
	Total	34	17	19	70	

Table 3: Cross-tabulation of RBS and POP score.

RBS	POP score			Total	p value
	Mild	**Moderate**	**Severe**		
Euglycemic	42	21	12	75	0.004*
Hyperglycaemic	2	4	9	15	
Hypoglycaemic	5	2	3	10	
Total	49	27	24	100	

*significant

Data wise 6 out of the 49 (12.2%) patients with mild grade of poisoning, 22 out of the 27 (81.4%) patients with moderate grade of poisoning and all the 24 (100%) patients with severe grade of poisoning required ventilator support and this was statistically significant (Table 2). This clearly demonstrates the validity of POP score in acute OP poisoning.

Total 75 out of the 100 patients enrolled had euglycemia,15 patients had hyperglycemia and 10 patients had hypoglycemia at admission.

Statistically 16% of euglycemics, 30% of hypoglycemics and 60% of hyperglycemics had severe grade of poisoning based on POP scoring and this was statistically significant (Table 3). Hence majority of hyperglycemics had severe grade of poisoning.

The ventilator requirements in hypoglycemics, euglycemics and hyperglycemics were 40%, 48% and 80% respectively (Table 4).

Among the euglycemics, 11 of the 36 patients who were intubated developed VAP and 15 developed MODS. Among the hyperglycemics, 10 of the 12 patients who were intubated developed VAP and 9 developed MODS. Among the hypoglycemics, 2 out of the 4 patients who were intubated developed VAP and 2 developed MODS.

Hence greater proportion of patients with hyperglycemia developed complications like MODS or VAP. The total atropine requirement was significantly greater among hyperglycemics than hypoglycemics or euglycemics. Mean duration of hospital stay among euglycemics, hyperglycemics and hypoglycemics were 7.23 days, 14.76 days and 9.63 days respectively, implying that hyperglycemics had the greatest duration of hospitalization (Table 4).

Table 4: Cross-tabulation of RBS and intubation rates.

Intubation	RBS-classified			Total	Chi-square value
	Euglycemic	Hyperglycaemic	Hypoglycaemic		
Not intubated	39	3	6	48	0.056
Intubated	36	12	4	52	
Total	75	15	10	100	

The overall mortality was 9%. In our study, mortality rate was highest with monocrotophos poisoning. 6 out of 75 (8%) euglycemics and 3 out of 15(20%) hyperglycemics succumbed to death (Figure 1). Hence proportion of deaths were greater in hyperglycemics than euglycemics or hypoglycemics.

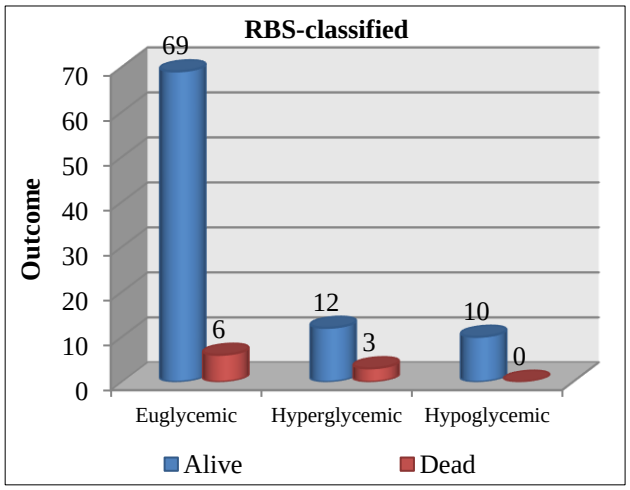

Figure 1: Cross-tabulation of RBS and mortality.

DISCUSSION

Statistically 100 patients with definite history of organophosphate poisoning were studied to assess glycaemic variability as a marker of poor prognosis. Hyperglycemia at the time of presentation, may be a harbinger of greater in-hospital mortality. Mechanisms include: Excess activation of nicotinic-N receptors resulting in excess catecholamine release (from sympathetic ganglia) and ACTH (from anterior pituitary), stress hyperglycemia and reduction in glucose induced insulin secretion by beta cells of Langerhans.

A prospective analytical study of 100 patients of acute organophosphate poisoning was conducted at Gujarat, Rajasthan and a few other states by Raghapriya et al, to assess glycemic status at the time of presentation as a prognostic indicator of clinical outcome. The cases were further categorised into hypoglycemics (37%), euglycemics (52%) hyperglycemic (11%). The outcome in terms of mortality was 59.45%, 9.6% and 63.63% in the respective groups. The ventilator requirements among the three groups were 94.59%, 53.84% and 100% respectively.[5]

In the present study conducted on 100 patients, majority of the patients (54%) were aged between 18 to 30 years with a male preponderance. The mode of poisoning was ingestion in all patients which was of suicidal intent. The most common presenting symptoms were vomiting, abdominal pain and excessive salivation. The most common presenting signs were bradycardia, tachypnoea, miosis and fasciculations. 49%,27% and 24% of patients enrolled had mild, moderate and severe grade of poisoning respectively. 75% patients had euglycemia,15% had hyperglycemia and 10% had hypoglycemia at admission. The ventilator requirement among euglycemics, hyperglycemics and hypoglycemics were 48%, 80% and 40% respectively. Also 16 % of euglycemics, 60% of hyperglycemics and 30% of hypoglycemics had severe grade of OP poisoning. Thus severity of poisoning and ventilator requirement were highest among hyperglycemics, correlating with the results of the study conducted by Raghapriya et al.[5] Overall mortality was 9%, with highest percentage of deaths occurred among hyperglycemics [3 out of 15(20%)] ,similar to mortality trends in the study conducted by Raghapriya et al.[5] The duration of hospital stay and duration of ventilation were also found to be prolonged among the hyperglycemics as compared to euglycemics or hypoglycemics.

A prospective observational study was conducted in Bangalore from January 2008 to December 2009 by Sudhir et al, to assess glycemic changes in acute anticholinesterase insecticide poisoning and to correlate with the severity of poisoning.[6] They concluded that a positive correlation exists between the glycemic changes and the severity of organophosphate poisoning; They also noted transient hyperglycemia associated with glycosuria

lasting for 3.25 days in OP poisoning group as compared to other insecticide groups. An observational study of 50 patients was conducted by Rao et al, in Hyderabad, to study the relevance of RBS levels in acute OP poisoning.[7] They concluded that hyperglycemia at admission was commoner than expected, in cases with moderate to severe poisoning. Hyperglycemia at admission correlates with depression of pseudocholinesterase levels in OP poisoning.

In the present study, pseudocholinesterase levels were suppressed in all the enrolled cases. However greatest levels of suppression (<500 U/L) were found in 9 patients, all of whom had severe grade of poisoning with 4 out of 9 having hyperglycemia at admission. This correlated with the findings of the study conducted by Rao et al.[7]

A prospective observational study was carried out in Cuttak, by Rachita et al, to assess the glycemic status of OP poisoned patients.[8] It concluded that a fall in serum cholinesterase value was more pronounced in patients having RBS >140 mg%, in parallel with severity of poisoning. Total atropine dose requirement was more for those patients having RBS >140 mg%, than those having RBS < 140 mg%. Majority of cases with hyperglycemia (57%) had severe grade of poisoning. The study also noted rise in the RBS at admission, serum malondialdehyde (MDA) levels, with a fall in the serum cholinesterase. These patients required more doses of atropine, indicating severity of poisoning.

A rare presentation reported by Jagadish Kumar of a 12 year old boy who presented as DKA which failed to improve with treatment.[9] However the boy went on to develop fasciculations with low pseudocholinesterase levels to support the diagnosis of organophosphate poisoning. The boy dramatically improved with atropine thus confirming the association of high blood sugars with the diagnosis of OP poisoning.

In the case reported by Swaminathan et al, a 15 year old girl was initially being treated for diabetic keto acidosis and after focussed evaluation was found to be a case of deliberate self-harm with acute organophosphate poisoning presenting as DKA who dramatically improved following administration of atropine and pralidoxime.[10] A similar unusual presentation of acute organophosphate poisoning as DKA was also reported by Shahid et at.[11] Thus, hyperglycemia in OP poisoning was associated with increased severity of poisoning, greater atropine dose requirement, greater intubation rates, greater incidence of complications like MODS/VAP, greater requirement of inotrope support, more indications for hemodialysis and significantly greater mortality.

CONCLUSION

Many factors contribute to the poor prognosis in OP compound poisonings. Hyperglycemia per se, is being considered as a factor to assess the severity of poisoning. The present study demonstrated the link between hyperglycemia and severity of OP poisonings. All parameters including ventilator support, duration of hospital stay, ICU complications and death were significantly high among hyperglycemics. RBS at admission in acute OP poisoning patients is a simple, inexpensive tool that may help to predict the clinical outcome. Early identification of the poor prognostic indicators may help in timely intervention/referral, so as to bring down the complications and mortality.

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